

## REMARKS

### **Amendments do not Introduce New Matter**

No new matter is introduced through entry of claims 3 through 10, and support for new claims 3 through 10 can be found in the specification as originally filed. More specifically, new claims 3, 4 and 5 find support, *inter alia*, in the specification on page 8, line 26 extending to page 9, line 15. New claim 7 finds support, *inter alia*, in the specification on page 8, lines 13-24. New claim 8 finds support, *inter alia*, in the specification on page 8, lines 13-24 and page 5, lines 9-32. New claims 9 and 10 find support, *inter alia*, in the specification on page 8, line 26 extending to page 9, line 22.

### **Priority**

The Examiner stated that the first line of the specification referred to expired provisional patent application 60/088,963, and that there was no reference to any other co-pending applications in the first line of the specification. Furthermore, the Examiner stated that no application data sheet was filed with the instant application. Therefore, under the provisions of 37 C.F.R. § 1.78 (a)(2), the Examiner asserts that the effective filing date of the instant application is the actual filing date, May 16, 2001.

Applicants note that the provisions of 37 C.F.R. § 1.78 (a)(3) state that [i]f the reference required by 35 U.S.C. 120 and paragraph (a)(2) of this section is presented in a nonprovisional application after the time period provided by paragraph (a)(2) of this section, the claim under 35 U.S.C. 120...for the benefit of a prior filed nonprovisional application...may be accepted if the reference identifying the prior application by application number ...was unintentionally delayed. A petition to accept an unintentionally delayed claim under 35 U.S.C. 120...for the benefit of a prior filed application must be accompanied by:

- (i) The surcharge set forth in § 1.17(t); and
- (ii) A statement that the entire delay between the date the claim was due under paragraph (a)(2) of this section and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional.

On October 07, 2002, Applicants petitioned the Commissioner to accord the instant application the status of a Divisional application of parent application 09/329,796, now U.S. Patent 6,291,174. The petition was filed in accordance with the provisions of 37 C.F.R. § 1.78(a)(3). On November 01, 2002, the petition under 37 C.F.R. § 1.78(a)(3) for an unintentionally delayed benefit claim was granted. Accordingly, the instant application is accorded the effective filing date of the parent application 09/329,796, now U.S. Patent 6,291,174, said effective filing date being June 10, 1998. A corrected filing receipt to that effect was included with the notice of decision on petition under 37 C.F.R. § 1.78(a)(3), both of which are included herewith for the Examiner's convenience.

### **Sequence Rules**

The Examiner objected to the specification as "this application fails to comply with the requirements of 37 C.F.R. 1.821-1.825 because there are disclosed sequences in the specification that are not properly identified." See Paper No. 3, Page 2, lines 25-26. Applicants have amended the specification to recite the proper Sequence Identifiers (SEQ ID NOs) corresponding to the disclosed sequences. Applicants respectfully request reconsideration and withdrawal to the objections to the specification under 37 C.F.R. §§ 1.821-1.825.

### **Rejections**

#### *Rejections under 35 U.S.C. § 112, 1<sup>st</sup> Paragraph*

The Examiner rejected claims 1 and 2 under 35 U.S.C. § 112, 1<sup>st</sup> Paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. More specifically, the Examiner asserts that

[t]he rejected claims are broadly drawn to methods for screening pigs to determine those more likely to produce larger litters and or those less likely to produce larger litters by determining which FSH  $\beta$ -subunit allele is present, of any possible FSH  $\beta$ -subunit alleles. Such a claim encompasses the use of any possible mutation or polymorphism in the FSH  $\beta$ -subunit that has a correlation with increased litter size in pigs. However, the specification only describes a

single polymorphism in the FSH  $\beta$ -subunit, a specific inserted retroposon allele, which was linked to litter size.

See Paper No. 3, Page 3, lines 15-21. The Examiner further states that “applicant has express possession of only one species in a genus which comprises at least hundreds of different possibilities.” See Paper No. 3, Page 4, lines 2-3. Additionally, the Examiner purports that “all of these claims encompass the use of different polymorphisms from those disclosed in the specification”, and that “[i]n the application at the time of filing, there is no record or description which would demonstrate conception of methods which utilize any polymorphism other than the single retrotransposon described in the specification.” See Paper No. 3, Page 4, lines 4-5 and lines 18-20.

Applicants respectfully disagree and traverse this rejection.

As an initial matter, Applicants note that the retroposon disclosed as SEQ ID NO:1 is a novel FSH  $\beta$ -subunit allele found to be strongly associated with litter size in pigs, as demonstrated by the genotype data presented in Table 1. More specifically, those individuals with the B allele (where the retroposon is absent) had increased litter size, demonstrating that the presence of the retroposon is negatively associated with litter size.

The Examiner appears to cite the *Fiers* and *Vas-Cath* cases for the proposition that applicants must provide a specific recitation of the structure of each of the additional FSH  $\beta$ -subunit alleles which may associated with pig litter size. The Federal Circuit in *Union Oil v. Atlantic Richfield*, however, held that for written description purposes “the primary consideration is factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. *Union Oil v. Atlantic Richfield*, 208 F.3d 989, 996 (Fed. Cir. 2000) (citing *In re Wertheim*, 541 F.2d 257, 262 (C.C.P.A. 1976). The court went on to state that “[t]he written description requirement does not require the applicant ‘to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.’” *Id* at 997 (citing *In re Gostelli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

Applicants assert that ample evidence exists in the specification as filed to demonstrate that applicants were in possession of the claimed subject matter at the time of the invention. More specifically, Applicants’ amended claims 1 and 2 are directed to a method of screening pigs to determine those more likely to produce large litters, which comprises determining the presence of at least one FSH  $\beta$ -subunit allele. As recited in the specification,

Applicants contemplated a method of identifying pigs more likely to produce large litters by “looking for particular DNA markers linked either directly or indirectly to the FSH  $\beta$ -subunit gene.” See specification, Page 3, lines 4-5. Importantly, Applicants are claiming a method of screening by identifying FSH  $\beta$ -subunit alleles shown to be associated with the FSH  $\beta$ -subunit allele of SEQ ID NO:1. Applicants are not claiming the specific DNA sequences of markers associated with FSH  $\beta$ -subunit allele(s), which according to the *Fiers* court as cited by the Examiner “requires definition of that substance other than by its functional utility.”

As stated by M. Slatkin, “LD [linkage disequilibrium] between a marker allele and the disease-associated allele decays as an exponential function of the product of time and the recombination rate, so markers currently in strong LD with a disease phenotype are likely to be very closely linked to the causative locus.” (Slatkin, M., “Disequilibrium mapping of a quantitative-trait locus in an expanding population”, *Am. J. Hum. Genet.*, 64:1765-73 (1999)). The Applicants also appreciated this concept in the instant application, which states that

[i]t is also possible to establish linkage between specific alleles of alternative DNA markers and alleles of DNA markers known to be associated with a particular gene (e.g. the FSH  $\beta$ -subunit gene discussed herein), which have previously been shown to be associated with a particular trait. In a further embodiment of the invention a number of such markers are used. For example, pairs of markers might be utilised to bracket the major gene to reduce any possible effects of recombination.

See specification, page 3, lines 2-17.

Once it is identified that additional markers of the FSH  $\beta$ -subunit gene have associations with litter size, it is straight forward for one skilled in the art to locate additional polymorphisms in this region, to determine the association between these polymorphisms and litter size, and to utilize these polymorphisms in a method in order to determine which pigs are preferred for this trait. As an example of routine experimentation in the art and to demonstrate that undue experimentation by skilled person would not be required, Applicants have enclosed a paper on association at single nucleotide polymorphisms in the *APOE* region (Martin, E., *et al.*, “Analysis of association at single nucleotide polymorphisms in the *APOE* region,” *Genomics*, 63:7-12 (2000)). This paper demonstrates that the level of information and skill in the art is such that, once one polymorphism is found, one of skill in the art can indeed detect additional polymorphisms by mere routine experimentation. Prior art

references already disclose at least two other FSH  $\beta$ -subunit alleles. Also, Linville *et al.* provides additional evidence that genetic variability in the FSH  $\beta$ -subunit gene may be associated with litter size (Linville, *et al.*, J. Anim. Sci., 77 (Suppl. 1): 131 (1999) (abstract enclosed)).

An example of the association of additional markers with a trait-enabling gene is provided by Rothschild, M., *et al.* (Rothschild, M., *et al.*, "The estrogen receptor locus is associated with a major gene influencing litter size in pigs", Proc. Natl. Acad. Sci. USA, 93:201-05 (1996)). Rothschild *et al.* demonstrated that the porcine estrogen receptor (ER) locus is associated with increased litter size. In making this determination, Rothschild *et al.* found that all markers and genes tested, except for one, "had some substantial linkages" to ER. See Rothschild *et al.* (Table 5 and the discussion of the results contained within Table 5). Similarly, Applicants have provided a specific allele demonstrated to influence pig litter size. Accordingly, one of skill in the art can take the teachings of the instant application and obtain additional markers associated with the FSH  $\beta$ -subunit allele of SEQ ID NO:1. Additional markers obtained in this manner are useful with the claimed method of screening to determine those pigs more likely to produce larger litters, and/or those less likely to produce larger litters.

Thus, Applicants have demonstrated that they were in possession of the claimed subject matter as of the effective filing date. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 1 and 2 under 35 U.S.C. § 112, 1<sup>st</sup> Paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

#### *Rejections under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph*

The Examiner rejected claims 1 and 2 under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. More specifically, the Examiner asserts that "[t]he claims do not set forth the relationship between the determining which FSH  $\beta$ -subunit allele(s) is present in the genome of individual pigs and determining those more likely to produce larger litters and therefore, it is not clear whether the claims are intended to be drawn to a method determining those more likely to produce larger litters or a method for determining which FSH  $\beta$ -subunit allele(s) is present in the genome of individual pigs.

Applicants have amended claims 1 and 2 herein in order to more distinctly recite the claimed subject matter. The amendments are introduced in order recite that the subject matter of the claims is drawn to a method of determining which pigs are more likely to produce larger litters. Applicants further submit that the claims are amended merely to clarify the language of the claim, and that the amendments do not change or effect the scope of the claims. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1 and 2 under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph in light of the claim amendments filed herein.

*Rejections under 35 U.S.C. § 102*

The Examiner rejected claims 1 and 2 under 35 U.S.C. § 102(b) as allegedly being anticipated by Yaofeng *et al.* (Science in China Series C Life Sciences, (Dec. 1998) Vol. 41, No. 6, pp. 664-668). More specifically, the Examiner asserts that

Yaofeng *et al.* Teach a method for screening pigs to determine those more likely to produce larger litters, and or those less likely to produce larger litters, which method comprises determining which FSH  $\beta$ -subunit allele(s) is/are present in the genome of individual pigs (p. 665). Yaofeng *et al.* employ methods which include the steps of (i) obtaining a sample of pig nucleic acid; and (ii) analyzing the nucleic acid obtained in (i) to determine which FSH  $\beta$ -subunit allele(s) is/are present. Yaofeng *et al.* specifically teach that this method 'will have a great consequence in swine breeding because the FSh  $\beta$  gene can be applied to marker-assisted selection to speed up the genetic improvement of litter size (p.668)"

Accordingly, the Examiner rejected claims 1 and 2 as allegedly being anticipated by Yaofeng *et al.* under 35 U.S.C. § 102(b).

Applicants respectfully disagree and traverse this rejection.

In order for a reference to anticipate under 35 U.S.C. § 102(b), the reference must disclose all limitations of the claimed invention in a printed publication in this or a foreign country more than one year prior to the date of application for patent in the United States. See MPEP § 2133 (emphasis added). Thus in order for Yaofeng *et al.* to be proper 35 U.S.C. § 102(b) art, all elements of the claimed invention must be described in the Yaofeng *et al.* publication in this or a foreign country more than one year prior to the date of application for patent in the United States.

Yaofeng *et al.* fails this test.

As stated *supra*, the instant application has been designated as a Divisional application of parent application 09/329,796, now U.S. Patent 6,291,174, and accorded the effective filing date of June 10, 1998. Yaofeng *et al.* published in December, 1998, and accordingly was not available as a publication in this or a foreign country more than one year prior to the date of application for patent in the United States in the instant case. Therefore, Yaofeng *et al.* is not available as proper 35 U.S.C. § 102(b). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1 and 2 under 35 U.S.C. § 102(b) as allegedly anticipated by Yaofeng *et al.*

#### *Double Patenting*

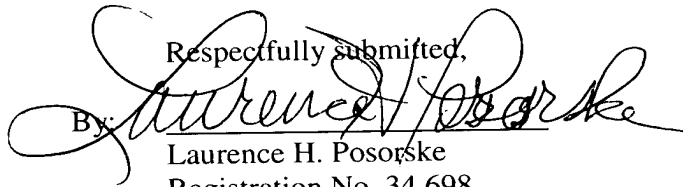
The Examiner rejected claims 1 and 2 under the Judicially created doctrine of obviousness-type double patenting, as allegedly being unpatentable over U.S. Patent No. 6,291,174.

Applicants respectfully submit that a terminal disclaimer in compliance with 37 C.F.R. § 1.321 will be submitted at such time as the allowable claims are agreed upon, excluding those claims subject to the double patenting rejection and thus requiring submission of the terminal disclaimer.

#### **Conclusion**

Applicants believe that incorporation of the amendments and consideration of the above remarks have placed this application in a condition for allowance. Early notification of a favorable consideration is respectfully requested.

Dated: December 5, 2002

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Hand Delivered December 5, 2002

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

TECH CENTER 1600/2900

**Application Number:** 09/855,682

**Examiner:** Einsmann, J.C.

**Filing Date:** May 16, 2001

**Art Unit:** 1645

**Title:** DNA markers for Pig Litter Size

**Inventor:** Li, N., *et al*

Commissioner of Patents and Trademarks  
Washington, D.C., 20231

**Appendix A – Version with Markings to Show Changes Made to the Specification**

At Page 1, line 2:

**--CROSS REFERENCE TO RELATED APPLICATIONS**

This application is a divisional application of Application No. 09/329,796, now U.S. Patent No. 6,291,174, filed June 10, 1999.--

At Page 3, lines 25-31:

--GGAGTTCCCCGTCGTGGCGCAGTGGTTAACGAATCCGATTAGGAACCATGAGG  
TTGCGGGTTCGGTCCCTGCCCTTGCTCAGTGGGTAAATGATCCGGCGTTGCATGA  
GCTGTGGTGTAGGTGTCAGACGAGGCTCGGATCCCCGCGTTGCTGTGGTTTCTGG  
CGTAGGCGGGTGGCTACAGTTTTGATTTCGACCCCTAGCCTGGGAACCTCCATATG  
CCGCGGGAGCGCCCAAAGAAATGGCAAAAGACGAAAAAAAAAAAAAAAAAAAAA  
AAAAAAAAAAAAAAAAAACGTTT (SEQ ID NO:1)--

At Page 4, lines 4-21:

--5'ttgagtttccatcggtggcgcaatggtaacgaatcgactaggaaccaagaggttgcgggttcgatccctggccttgctcagt  
gggttaaggatccagcattgctgtgagctgtggtgttaggttacagacacagcttgatcccacgttgctgtggccctggcatagggcga  
tggttacagctctgattagaccctagccttggaactccatatgccaaggagcagtcgaagaaatggcaaaaagacaaaaaaa  
agttttcttttaataaaatgttttaaatgataatgaaggacaaatgatgatcacaattacttgcttcagagtaatcctttaagacagtc  
aatggcaatactctataaatattgctctgcttcaaacattatattggagtttgaccataatatagttactttgacaaaaaaaaaaaaa



tgaggaggagaataagaagaacgttttGGAGTTCCCCGTCGTGGCGCAGTGGTTAAACGAATCC  
GATTAGGAACCATGAGGTTGCGGGTTCGGTCCCTGCCCTTGCTCAGTGGGTTAAT  
GATCCGGCGTTGCATGAGCTGTGGTGTAGGTTGCAGACGAGGCTCGGATCCCCGC  
GTTGCTGTGGTTTCTGGCGTAGGCGGGTGGCTACAGTTTTGATTGACCCCTAGC  
CTGGGAACCTCCATATGCCGCGGGGAGCGCCCAAAGAAATGGCAAAGACAGA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGAACGTTTgttcaagaacaaagaattaaag  
aaaaggaaaaggaaggaaaaaccactataggagtaaaatgtgactggagaggatgaatagaccagttattcaaggttggtaactta  
cattacgaatgtaattctttggtttttcagtttttacaggcctaattgtttggtttccacccaagatgaagtcgctgcagtttgcctcatt  
ctgttgctggaaagccatctgctgcaatagctgtgagctgaccaacatcaccatcacagtggagaaagaggagtgaacttctgcataa  
gcatcaacaccacgtggtgtgctggctattgctacaccgggtaggttctttgcttagaagtgagggtgctgaaggtctgtaaag  
gcgggctttactaattcccc-3' (SEQ ID NO:2)--

At Page 5, lines 12-13:

--forward: 5' CCTTTAAGACAGTCAATGC 3' (SEQ ID NO:3); and  
reverse: 5' ACTGGTCTATTCATCCTCTC 3' (SEQ ID NO:4)--

At Page 10, lines 7-8:

--forward: 5' CCTTTAAGACAGTCAATGC 3' (SEQ ID NO:3); and  
reverse: 5' ACTGGTCTATTCATCCTCTC 3' (SEQ ID NO:4)--



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TECH CENTER 1600/29

**Application Number:** 09/855,682

**Examiner:** Einsmann, J.C.

**Filing Date:** May 16, 2001

**Art Unit:** 1645

**Title:** DNA markers for Pig Litter Size

**Inventor:** Li, N., *et al*

Commissioner of Patents and Trademarks  
Washington, D.C., 20231

**Appendix B – Version with Markings to Show Changes Made to the Claims**

Claim 1:

--1 (amended). A method for screening pigs to determine those more likely to produce larger litters, and/or those less likely to produce larger litters, ~~which~~ wherein the method comprises determining the presence of at least one marker linked to the ~~which~~ FSH  $\beta$ -subunit allele(s) of SEQ ID NO:1 is/are present in the genome of individual pigs, and wherein said marker is associated with pig litter size.--

Claim 2:

--2. (amended). ~~A The method for screening pigs to determine those more likely to produce larger litters, and/or those less likely to produce larger litters~~ of claim 1, which wherein said method comprises the steps of:

- (i) obtaining a sample of pig nucleic acid; and
- (ii) analysing the nucleic acid obtained in (i) to determine the presence of at least one marker linked to the ~~which~~ FSH  $\beta$ -subunit allele(s) ~~is/are present~~ of SEQ ID NO:1 in the genome of individual pigs, and wherein said marker is associated with pig litter size.--